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Adverse Childhood Events and Psychosis in Bipolar Affective Disorder

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Abstract

Background: There has been increasing interest in the association between childhood trauma and psychosis. Proposals for potential mechanisms involved include affective dysregulation and cognitive appraisals of threat, yet few large-scale clinical studies exist in affective psychosis.

Aim: We hypothesise that within bipolar disorder (BD), childhood events will show a significant association with psychosis, and in particular with symptoms driven by dysregulation of mood or with a persecutory content.

Method: 2019 participants were recruited as part of our programme of research into the genetic and non-genetic determinants of BD (www.bdrn.org). Data on lifetime ever presence of psychosis and specific psychotic symptoms were determined by detailed structured interview with case note review. Childhood events were recorded after self-report questionnaire and case note information.

Results: There was no relationship between childhood events, or childhood abuse, and psychosis per se. Childhood events were not associated with an increased risk of persecutory or other delusions. Significant associations were found between childhood abuse and auditory hallucinations, strongest between sexual abuse and mood congruent or abusive voices. These relationships remain significant even after controlling for lifetime ever cannabis misuse.

Conclusions: Within affective disorder, the relationship between childhood events and psychosis appears to be relatively symptom-specific. It is possible that the pathways leading to psychotic symptoms differ, with delusions and non-hallucinatory symptoms being influenced less by childhood or early environmental experience.

Key Words: Childhood Life Events, Psychosis, Bipolar, Hallucinations, Delusions

Declaration of Interest: None

1. Introduction

In recent years a number of studies have investigated an association between the presence of psychotic symptoms and a history of childhood trauma. A recent meta-analysis of thirty-six studies concluded childhood adversity increases the risk of psychosis nearly three-fold (1). Some authors now propose a causal relationship between these early childhood events and the subsequent development of schizophrenia (2, 3), and this association has influenced key cognitive models of psychosis. One example is the proposal that adverse experiences in childhood will lead to the development of negative schemas of the self and the world (the self as vulnerable and others as dangerous) which facilitate the development of paranoid delusions (4). Furthermore, Birchwood et al. suggest that childhood experience of social adversity leads to the development of negative schemas involving social humiliation and subordination, which in turn may fuel paranoia (5). Alternatively, within biological models of schizophrenia the experience of abuse is proposed to create vulnerability to psychosis through heightened stress reactivity and cortisol dysfunction (6, 7). In addition, affective dysfunction following childhood trauma is increasingly highlighted as a mechanism through which psychosis develops (3, 8). However, this analysis, and much of the literature to date, focuses on non-affective psychosis or data from population based studies with subclinical psychotic-like experiences (1, 2, 9-11). We know that childhood trauma is also associated with a wide number of adverse outcomes, for example depression, suicidal behaviour, personality disorder and bipolar disorder (12). Affective dysfunction is also proposed as a mechanism to explain these associations. For example, Etain et al suggest that a dual role of genetic and environmental influences of socially and morally inappropriate rewards and parental attitudes during childhood induces affective dysregulation in the developing child that precedes the development of bipolar disorder (13, 14). Thus, given that childhood trauma is proposed as a risk for psychosis and affective dysfunction, it is surprising that few studies have investigated the role of childhood trauma in psychotic symptoms as part of an affective disorder to date.

In addition childhood trauma itself encompasses many experiences, however few studies have investigated specific life events in detail. In one study Bentall et al looked at this issue in a large population based sample and found that sexual abuse was associated only with hallucinations, whereas being brought up in institutional care was associated with “paranoia”. They proposed the specific associations observed were consistent with current psychological theories about the origins of hallucinations and paranoia (15).

Our study sought to build and expand the current evidence base by exploring the association between a range of adverse childhood events and the presence of psychotic symptoms in a very large, well-characterized sample of patients with bipolar disorder (BD). We hypothesise that for individuals with affective disorder, childhood trauma will show a significant association with psychosis, and in particular with psychotic symptoms coupled with dysregulation of mood (ie mood congruent delusions and hallucinations) and with a persecutory or abusive content.

2. Methods

The study was part of our on-going programme of research into the genetic and non-genetic determinants of BD and related mood disorders (Bipolar Disorder Research Network, BDRN; www.bdrn.org) which has UK National Health Service (NHS) Research Ethics Committee approval and local Research and Development approval in all participating NHS Trusts/Health Boards. In light of the potential distress caused by the subject matters involved in this study, ethical approval and study methods included information on how to access support helplines from the charity Bipolar UK UK-based user-led charity and telephone access to the study team which includes experienced clinicians with the ability to access local help as needed. The Childhood Life Events Questionnaire (CLEQ) was not asked until towards the end of the 1 ½ interview to ensure researchers had time to establish rapport with participants before asking about events occurring in their childhood. Researchers also took the time to explain to participants why these events are being asked about. In many cases, events occurring in childhood were disclosed by the participant to the researcher before the CLEQ was asked as participants felt these events had played a role in the course of their mood illness. In addition, throughout the interview participants could ask the interviewer to move onto another question, take a break or end the interview at any time. Each researcher also had sufficient training and experience to provide the necessary support and advice to participants who experienced distress following the interview.

2.1 Sample

Participants were recruited via both systematic and non-systematic recruitment methods. Participants are recruited systematically through NHS psychiatric services (community mental health teams and lithium clinics) and non-systematically using advertisements for volunteers via the research team websites, leaflets, posters, media coverage and through the, Bipolar UK. The research programme inclusion criteria require participants to be;

a) 18 years or over
b) able to provide written informed consent
c) their affective disorder not to be the result of alcohol/substance abuse or dependence, medical illness or medication
d) not biologically related to another study participant
e) UK White British due to the research programme focus on genetic analysis.

This current study was conducted on a subset of participants who had a DSM-IV diagnosis of bipolar I for whom data on adverse childhood events had been collected. Given the focus on affective disorder and psychosis, we excluded those with a diagnosis of bipolar II, where psychotic symptoms would be less likely to occur (16).

2.2 Data Collection

Clinical data were collected using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) semi-structured interview (17). This was supplemented by reviewing participants' psychiatric case notes. Data were combined to make best-estimate lifetime-ever diagnoses according to DSM-IV and to rate lifetime-ever clinical characteristics. This included age at illness onset, lifetime alcohol and substance use and the lifetime presence/absence of specific delusions (including persecutory, grandiose, depressive, nihilistic, guilt, and reference); auditory hallucinations (including mood congruent hallucinations, accusatory/abusive and running commentary) and visual hallucinations (including all visual and mood congruent visual hallucinations).

Inter-rater reliability was high. Mean kappa statistics were 0.85 for DSM–IV diagnoses and ranged between 0.81 and 0.99 for other key clinical categorical variables; mean intra-class correlation coefficients were between 0.91 and 0.97 for key clinical continuous variables.

Adverse childhood events were assessed by asking participants, via the Childhood Life Events Questionnaire (CLEQ; see data supplement 1), if they had experienced one or more of a list of 13 adverse childhood events before the age of 16 including separation/re-marriage of parents, the death of a parent, friend or sibling, hospitalisation/ jail sentence of a parent and being suspended from school. Information specifically for childhood abuse events were collected from a number of sources including the CLEQ. In the CLEQ childhood abuse and bullying are not specifically asked about, however participants are given the opportunity to disclose additional events by being asked "Are there any other significant life events you experienced as a child that are not mentioned above?" Case notes were also reviewed for any mention of adverse child events including abuse and bullying. In addition participants completed the Brief Life Events Questionnaire with an open question included asking for details of any other life event- this was also examined for evidence of childhood events (18).

2.3 Statistical Analysis

Individuals were grouped according the lifetime presence or absence of psychosis as defined by the presence or absence of any type of delusion or hallucination. Demographic and clinical characteristics of the groups with and without psychosis were compared using a chi-squared test of association and independent samples t-test as appropriate.

We examined the association of childhood events with psychosis in general and then specific psychotic symptoms; the presence or absence of grandiose delusions, depressive delusions (including nihilistic delusions, delusions of guilt and/or delusions of poverty) and persecutory delusions; mood congruent auditory and visual hallucinations, and 2nd person abusive/accusatory or 3rd person/running commentary auditory hallucinations.

Individuals were grouped as either having suffered any adverse childhood event or not. The 13 types of childhood events were then grouped into the 5 most frequent categories; childhood abuse (CA), death of a loved one, victimising events (including bullying), family

disruption (including parental separation) and difficulties at school. CA was then further classified into sexual (CSA), physical (CPA) and emotional (CEA) abuse.

Chi square tests of association were used to explore the relationship between lifetime history of experiencing childhood events, psychosis and specific psychotic symptoms. For categories with significant association, odds ratios (OR) with 95% confidence intervals were calculated, using forward stepwise logistic regression. OR's were adjusted to account for lifetime-ever cannabis use, as there is considerable evidence of the role of this confounding variable in the mediation of trauma and psychosis (19,20), gender, age at interview and age of onset. Previous studies have commented on the increased risk of childhood sexual abuse and psychosis in females (21). Data analysis was performed using the SPSS 20.0 package for Windows.

3.0 Results

3.1 Demographic and clinical characteristics

The final sample consisted of 2019 participants with a mean age of 47 years. 70% (N=1415) were female. 70% (N=1408) had a lifetime history of any psychosis. The participants with psychosis were more likely to be female ($\chi^2$6.5 (1) p=0.01), younger at interview (t=-4.7, p=0.007) and have an earlier age of illness onset (t=-3.08. p=0.002)

75% (N=1499) of participants in the sample reported experiencing one or more adverse childhood event. In addition, 17% (N=349) reported two different categories of adverse event, 9% (N= 177) reported three and 3% (N= 66) reported 4 or more types of adverse event. A history of life time ever cannabis use was significantly associated with any childhood event (χ2 10.6, p=0.001).

Please see Table 1 for further details.

3.2 Childhood Events and association with Psychotic Symptoms

Initial analysis showed that having experienced any childhood event, or childhood abuse, was not significantly associated with having a history of psychotic symptoms (any childhood event: X^2 0.02, p= 0.46; CA X^2 0.07, p=0.42).

3.3 Delusional Beliefs

There was no significant association between childhood events and having a life time ever history of delusions (X^2 0.19, p=0.53). Childhood events were also not significantly associated with persecutory or depressive delusional beliefs. However, subsequent individual analysis showed a significant association between CA and grandiose delusions, such that

individuals with a history of childhood abuse had lower risk of developing grandiose delusions (OR 0.68, p = 0.03). Analysis of the subtypes of childhood abuse demonstrated that this relationship held true for both childhood sexual abuse (OR 0.66, p = 0.02) and childhood physical abuse (OR 0.66, p =0.03).

See Table 2 and 3 for full details.

3.4 Auditory Hallucinations

There was a significant association between childhood events and mood congruent auditory hallucinations ($\chi 2$ 8.57, $p<0.01$, OR 1.55). This association was driven primarily by the CSA subcategory, which remains significant after controlling for lifetime ever cannabis use, gender, age at interview and age of onset of illness (O.R 2.56, $p <0.0001$).

Death of a loved one was significantly associated with mood congruent auditory hallucinations ($\chi 2$ 6.07, $p<0.01$, OR1.37, $p<0.05$) as was experiencing a victimising event ($\chi 2$ 9.07, $p<0.001$, OR 1.55, $p<0.01$).

CA was also significantly associated with experiencing abusive/accusatory hallucination content. This association was strongest for CSA ($\chi 2$ 125.88, $p<0.001$, OR 2.45), however CEA was also associated with abusive/accusatory hallucinations ($\chi 2$ 4.31, $p<0.05$) as was experiencing a victimising event (X2 11.26, $p<0.001$). The association between auditory hallucinations and CEA or victimising events did not remain significant after controlling for lifetime ever cannabis use, gender, age at interview and age of onset of illness.

See Tables 2 and 3 for full details

3.5 Visual Hallucinations

CA, CSA, CPA and CEA were significantly associated with mood congruent visual hallucinations ($\chi 2$ 8.80, 10.33, 4.48, and 4.04 respectively, $p<0.05$-0.01). These associations remained significant after the influence of age, gender, and cannabis use is controlled for CA (O.R. 1.90), CSA (O.R. 2.09) and CPA (O.R. 1.81).

See Tables 2 and 3 for full details.

3.6 Cumulative Effect of Multiple Childhood Events

The association between experiencing multiple types of childhood life events and psychosis was then considered. The greater the number of different adverse events experienced the greater the odds of developing any auditory hallucinations, abusive/accusatory or mood congruent hallucinations (see fig 1).

4.0 Discussion

We hypothesised that in patients with bipolar disorder, adverse childhood events, would show a significant association with psychosis, and in particular with symptoms driven by dysregulation of mood (mood congruent delusions and hallucinations) or with a persecutory or abusive content. Our hypothesis was only partially upheld. Childhood trauma, or any type of adverse childhood event, was not associated with overall psychosis. We demonstrated significant associations between childhood abuse and hallucinations which are mood congruent, or with an abusive content. These type of hallucinations remain highly significantly associated with childhood sexual abuse even after controlling for lifetime ever cannabis misuse. Significant associations were also found for other types of adverse childhood life events, including death of a loved one and experiencing a victimizing event, including bullying, and hallucinations. We did not find an increased risk of delusional beliefs, persecutory or depressive delusions, after any form of childhood event.

The strength of this study includes the detailed clinical information available on a large number of participants. This level of detail, in terms of specific psychotic symptoms and range of childhood experiences has not been reported before in such a large clinical sample. This has also allowed controlling for the effects of cannabis use, one of the main confounding variables potentially mediating the effects of childhood adversity on the presence of psychosis, gender and age of illness onset. Numerous studies report the frequency of substance misuse following childhood abuse, and the influence of cannabis on precipitating and causing psychosis is now clear (22, 23). The role of substance misuse in psychosis within BD has also been previously proposed as an important factor in mediating poor outcome (24). However over and above this we have found that childhood abuse is a potentially significant factor in the risk for hallucinations, and in addition that experiencing multiple types of childhood event substantially increased risks.

4.1 Hallucinations

When looking at auditory hallucinations individually, previous research supports the existence of a relationship with childhood trauma, such that in their 2005 review Read et al conclude there is likely a causal relationship between child abuse and hallucinations(2). This statement has been criticised as being over-ambitious (10) but many papers have reported similar findings (1, 2, 6, 25). The majority of this research concerns childhood abuse and the findings tend to show childhood emotional and sexual abuse are the most notable forms of abuse associated with auditory hallucinations; Daalman et al found that psychotic patients with auditory verbal hallucinations were 3 times more likely to be victims of childhood sexual abuse and over 5 times more likely to have suffered emotional abuse than healthy controls (26). Shevlin et al demonstrated that childhood sexual abuse is significantly related

to both auditory and visual hallucinations and that experiencing multiple types of trauma increases the likelihood of having hallucinations (27).

Thus our results confirm that previous reports are also now relevant to affective psychosis, and add to the weight of evidence of the importance of childhood adversity in increasing the risk of experiencing hallucinations with data from our large clinical sample. Additionally, until now no studies have looked at the form or content of auditory hallucinations in as much detail as our extensive data set allowed. It is interesting that traditionally Scheiderian first rank hallucinations of voices speaking in a running commentary were not associated with any type of childhood trauma. It is possible that first rank symptoms of schizophrenia, linked to a more negative outcome within psychosis, may be less determined by early environmental influences, and possibly have a more genetic, prenatal or epigenetic aetiology (28).

Association between visual hallucinations and child abuse is also interesting. The suggestion may be one that post traumatic symptomatology is more relevant with mood congruent visual imagery, and flashbacks seen within the context of an abusive past. PTSD symptoms in psychosis are increasingly recognised; and the phenomenology and pathophysiology may not be as distinct as first proposed (29).

4.2 Delusional Beliefs

The evidence for an association between delusional beliefs and childhood trauma is much less developed than that for auditory hallucinations, since few studies have looked at delusions specifically. Read et al compared 60 patients with psychosis to controls and found the presence of delusions was not related to any form of childhood abuse (30). Conversely, Saha et al found that delusional-like experiences were significantly associated with trauma (31). Indeed, of the small number of papers specifically examining delusions, the majority found no significant association between childhood trauma and delusional beliefs (1). Our results in the largest clinical study of delusions as a discrete symptom concur with this. We found no significant relationship between any adverse childhood events, and specifically childhood abuse, and depressive or persecutory delusional beliefs. This will thus question the role of childhood trauma in the development of delusions. This is somewhat counter-intuitive to the accepted cognitive models of the development and maintenance of persecutory beliefs, which are proposed as the result of hyper-vigilance, increased threat to self and cognitive bias of perceived victim status (4, 32). Many studies investigating the effect of psychological therapies in persecutory ideation, often with mixed results, have this model as their basis (33). Our results do not support a role of childhood trauma as a risk for persecutory or depressive delusions in bipolar disorder, suggesting perhaps that the cognitive bias underlying delusions may stem from later experience, or indeed be more biologically driven.

We did find that childhood abuse had an inverse association with grandiose delusions, a novel finding not previously demonstrated. One possible explanation is that once abuse is experienced, self-esteem or self-belief is so challenged that one is never able to generate grandiose content, even within the context of an elevated mood.

4.3 Full range of Childhood events and Psychosis

Some previous studies have identified the association between psychosis and wider experiences such as spending time in care, parental loss or separation and victimising events such as bullying (34). However, again most were community-based and measured sub-clinical symptoms. Consequently, until now, only childhood abuse has been mainly considered when investigating childhood life events and psychosis. Nevertheless, our data support the suggestion that, while childhood abuse, in particular childhood sexual abuse, may be the most significant trauma in relation to later experience of hallucinations, other events such as experiencing a victimising event or the death of a loved one are also extremely relevant.

Bentall et al recently investigated whether specific life events were related to specific psychotic symptoms in a large population based sample and found that childhood sexual abuse was associated only with hallucinations, alternatively being brought up in institutional care was associated with "paranoia". They proposed the specific associations observed are consistent with current psychological theories about the origins of hallucinations and paranoia (15). However, the effect sizes we report suggest that, in those with a diagnosis of bipolar disorder in adulthood, earlier childhood events, and even childhood sexual abuse, may only have a moderate impact on the risk of experiencing hallucinations, and no impact on delusions. A number of other previous studies report significant associations between childhood trauma and psychosis far stronger than this. Most of these studies are from community-based samples with broad definition of psychosis and classified by self-report (1). This may suggest that sub-clinical or informally diagnosed symptoms, such as hearing brief "voices", having persecutory-like experiences or "paranoia", are quantifiably different to formally diagnosed psychotic symptoms, at least within bipolar disorder.

4.4 Limitations

Our findings have limitations which should be taken in to consideration. Child abuse was not asked about directly during interview but relied on case note information and open questions on the CLEQ and BLEQ questionnaires. Therefore the prevalence of childhood abuse in our sample may be underestimated; however our prevalence rates of near 20% for childhood abuse are comparable to other literature (22, 24). Another important consideration is the retrospective and cross sectional nature of data collected, which relies on recollection. Many lay people are aware of a link between mental illness and ones upbringing, especially abusive circumstances. Therefore, having been diagnosed with bipolar disorder, participants may look back and scrutinise their childhood years for evidence of abuse, which they otherwise would not have considered. However, the prevalence of abuse reported in our sample does not appear to be in keeping with this. We are careful not to over emphasise the associations demonstrated, and whist we can speculate on underlying mechanisms, clearly a direct causal effect has not been demonstrated within this cross sectional study and further detailed study is

required before firm conclusions can be drawn regarding associations between childhood adversity, mood dysregulation and psychosis. Finally, some less common psychotic symptoms, for example disorders of thought or passivity experiences, were not examined.

4.5 Conclusions

Our findings are consistent with the current evidence that childhood abuse is significantly associated with later auditory and visual hallucinations, but not delusions. This suggests that the relationship between childhood events and psychosis may be symptom-specific. Given the increasing overlap between affective and non-affective psychosis and the increasing role affect is given in the development of psychosis, this will have relevance through the whole psychosis spectrum (35, 36). It is clear that childhood adversity has a negative impact on the course of affective disorder (37) and our results suggest that in part this may be due to a heightened risk of experiencing hallucinations. It is possible that the pathways leading to specific psychotic symptoms differ, with delusions and non-hallucinatory symptoms being influenced less by childhood or early environmental experience. Future research exploring the relationships between childhood experience and psychosis will need to clarify whether this pattern is replicated across the clinical psychosis spectrum. More importantly, however, may be the need for increasing phenomenological detail for type and subclass of delusion, hallucinations as well as type and impact of childhood trauma when investigating risk factors for psychosis. We have shown that these risks may well be different for each symptom domain. Increased knowledge here has the potential to help identify those at heightened risk and aid provision of beneficial treatment, for example with increased early and novel treatments for hallucination related cognitive distortions such as those targeting inner speech self-monitoring, in those known to have experienced childhood trauma (38). Finally, this detailed knowledge of the specific symptom risks has the best potential to improve our understandings of what “causes” psychosis.

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